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EP-A- 0 104 696
FR-A- 2 070 888
FR-A- 2 240 866
US-A- 3 837 353
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ADVANCES IN INSTRUMENTATION, vol. 36,
part 2, 1981, pages 27-44, ISA; M. VASEL:
"Variable speed pumping for level control"

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Description

The present invention relates to an apparatus for the continuous filling of flexible bags or pouches with a perfusion liquid from a source of such liquid, the apparatus including means for regulating the flow rate of the perfusion liquid coming from the reservoir, as a function of the liquid's level in the reservoir.

There is already known an apparatus of the type described above. In that known apparatus, which is of the mechanical type, the liquid level in the reservoir is maintained near a pre-set level, by means of a float that operates a valve or mechanism for closing the duct which feeds perfusion liquid to the reservoir.

The known apparatus however suffers several disadvantages. One disadvantage is that the apparatus does not allow the bags or pouches to be filled with a precise volume of perfusion liquid, especially when that liquid is viscous. Using the known apparatus proves inefficacious when the perfusion liquid contains more than 50% dextrose.

Moreover, the known mechanical device generates solid particles in the perfusion liquid, which may reach sizes that exceed those acceptable to the pharmacopeiae.

Furthermore, the volumes of perfusion liquid introduced into the bags or pouches may vary by as much as approximately 10% of the required volumes when the known mechanical apparatus is used.

The present invention remedies these drawbacks.

The apparatus of the invention, of the type defined above in the present specification, is characterized in that the afore-mentioned regulating means comprise a sensor mounted in the reservoir which sends a signal as a function of the liquid level in the reservoir, and which is connected to a regulator that continuously regulates the feeding of the perfusion liquid to the reservoir as a function of the electronic signal, the sensor and regulator together operating to maintain the liquid level in the reservoir near a pre-set level.

A feature of the invention is that the afore-mentioned regulator is a regulator with proportional, integral and derived action, which transforms a signal received from the sensor into a governing signal for a member feeding perfusion liquid to the reservoir, that member preferably being a device varying the speed of a pump which feeds perfusion liquid to the reservoir.

Another feature of the invention is that the sensor is connected to the transformer of the signal sent by that sensor into an electric current the intensity of which ranges between 0 to 20 milliamperes, which current is sent to the regulator.

US 3837 353 discloses an apparatus and method for controlling the level of oil in a surge drum in an oil refining process. The apparatus makes a calculated charge to the flow rate of charge oil entering the hydrotreater upstream of the surge drum at same time prior to a charge in the catalytic reforming unit charge oil flow rate downstream of the surge drum.

Other features and details of the invention will be apparent from the following description which refers to the single figure of the attached drawing, same schematically representing an embodiment of the device of the invention.

The apparatus shown in the drawing is designed to maintain a level 1 approximately equal to a pre-set value inside a reservoir 2 of perfusion liquid.

The perfusion liquid is fed from a storage tank 3 and is brought into the reservoir 2 via a duct 4, after filtration through a filter 5 and with the aid of a pump 6.

The liquid contained in the reservoir 2 for this part is fed continuously by gravity through a duct 7 and into a bag or pouch 8.

A sealing mechanism 9 brings the internal walls 10 of the bag or pouch 8 against each other before sealing them together.

The desired volume of perfusion liquid is obtained by a full-cycle of the machine, which corresponds to the time necessary for the forward motion of the pouch or bag 8 in the direction indicated by arrow x, and the time necessary for the sealing together of the walls and for the moving away of the wall sealing mechanism from the walls 10 of the pouch 8.

The bags or pouches 8 are severed at the opening of the sealing mechanism 9, that is to say when said mechanism moves away from walls 10 of the bag or pouch 8.

The bags or pouches 8 are obtained from a continuous sheet 11 of either polyethylene or polypropylene, the lateral edges 12 of which are sealed to each other or on each other.

The rate of flow of the liquid entering the pouch is, among other things, a function of the viscosity of the liquid and of the level of liquid in the reservoir 2.

That rate of flow must be such that it is possible to fill the pouch 8 with a pre-set volume during a cycle of the sealing mechanism 9.

The apparatus of the invention makes possible, without varying the speed of intermittent forward motion

(arrow x) of bags or pouches 8, to fill with great precision those bags with transfusion liquids the viscosities of which may be different.

That speed of discontinuous forward motion of the bags or pouches requires the filling of those pouches to be carried out over a determined period of time. Therefore, the sole remaining parameter to maintain a constant rate of flow of a perfusion liquid having a given viscosity, is the height of the liquid level in the reservoir 2.

That level may be kept near a pre-determined value or mandatory level, by means of an automatic regulation device indicated by numeral 14.

The automatic device includes regulating means comprising a sensor 15 which sends an electric signal as a function of the liquid level in the reservoir 2 and which is connected to a regulator 16 which continuously regulates the supply to the reservoir 2 of perfusion liquid coming from tank 3, so as to maintain the liquid level in reservoir 2 near the mandatory level.

Sensor 15, preferably, is a capacity-type sensor, although it may also be a resistance-thermal-, or piezo-electric-type sensor.

The capacity-type sensor 15 may include, in a manner known in itself, two concentric cylinders that serve as electrodes, the external cylinder having holes near its base allowing a free circulation of the liquid between the two cylinders. The sensor 15 determines an electric capacity which varies either in a linear or in a logarithmic manner with the liquid level in the reservoir 2.

The signal sent by the sensor 15 is modified by a transformer 17 into a current the intensity of which ranges between 0 and 20 milliamperes.

In a preferred embodiment, the transformer 17 modifies the signal sent by the sensor 15 into a current the intensity of which ranges between 4 to about 20 milliamperes, so as to alert the user of the possible stopping of the transformer 17.

The electric current sent by the transformer 17 is introduced into a regulator 16. The regulator 16 preferably is a continuous regulator with proportional, integral and derived action (PID) which measures the deviation between the level determined by sensor 15 and the mandatory value of that level, and which produces a signal the intensity of which is partly proportional to the measured deviation, partly proportional to the integral of the deviation measured over time, and in part proportional to the derivative of the deviation measured over time.

The regulator 16 of the PID type allows the production of a signal which is sent into a member for the feeding of reservoir 2, that member being made up of a device 18 for varying the speed of pump 6 which advantageously is a centrifuge pump.

The device 18 for varying the pump speed includes a converter 19 which transforms the signal coming from the regulator 16 into a variation in the speed of the pump 6, proportional to the rate of flow and to tolerance.

The filter 5 mounted inside the duct 4 downstream from the pump 6 and upstream from the reservoir 2, is inserted between two pressure sensors 20 which send electric signals to a device 21 that compensates for the loss of charge in the filter 5. The compensating unit 21 is mounted upstream from the converter 19 and downstream from regulator 16. The compensating unit 21 permits the regulation of the speed of the pump 6 as a function of the degree of clogging of the filter 5.

The filter 5 is designed to retain the solid particles present in the perfusion liquid at the exit of the pump.

The filter 5 makes it possible, because of its high loss of charge, to prevent any syphoning from either tank 2 or 3 toward the other tank 3 or 2 when the operation stops or starts.

Obviously, the PID regulator 16 may also take into consideration other parameters to maintain the level of the perfusion liquid near a pre-set value.

For example, the PID regulator 16 may receive a signal coming from a level sensor and a signal coming from a temperature sensor. The latter signal makes it possible to correct errors resulting from a change in the viscosity of the fluid or in its dielectric constant, with temperature.

Bag filling tests were carried out with an apparatus according to the present invention.

In that device, the signal sent by the capacity-type sensor 15 was modified in a transformer 17 into an electric current with an intensity ranging between 0 and 20 mA. That maximum current intensity corresponded to a maximum variation of the liquid level in reservoir 2, which was equal to 13.75 cm.

The PID type regulator 16 had a gain of 30% and a time differential of zero.

The device 18 for the variation of the rotation speed of the pump 6 had an acceleration and a deceleration time equal to 10 seconds. It received an electric signal with an intensity ranging between 0 and 20 mA which, once transformed, made it possible to obtain a rotation speed for the pump 6 ranging between 0 and 3600 rpm.

A valve 22 was placed on duct 7 allowing liquid to flow into the pouches 8. The valve 22 served to limit or stop the flow of liquid out of reservoir 2, when the operation of the apparatus was stopped. The reservoir 2 had a vent 23 the end 24 of which was located inside a sterile atmosphere.

These tests were carried out for the filling of pouches or bags 8 with nominal capacities of 250, 500 and 1,000 milliliters, respectively.

Perfusion liquid was introduced into 250 ml pouches. The response times of the regulator 16, at 1% of the mandatory value, were 20 seconds at the start of operations, and 10 seconds for passing from one mandatory value to another (deviation between mandatory values: 10%).

The pouches or bags with a nominal capacity of 250 ml received, on the average, 265.25 ml, to account for losses by evaporation during sterilization of the product, as well as for errors resulting from filling.

The typical deviation calculated for 200 pouches was 0.447 ml that is to say a variation of 0.168%.

A second series of tests on 200 pouches gave the following results:

--- Average value of the content	264.76 ml
--- Typical deviation	0.575 ml
--- Variation (Typical deviation over average content)	0.21%

Filling tests for bags or pouches 8 of 500 ml were carried out with a regulator 16 which, at 1% of the mandatory value, had a response time of 6 seconds at the start of operation, and of 9 seconds for passing from one mandatory value to another.

The results obtained are set forth in Table I below:

T A B L E I

Test No.	Number of Pouches Tested	Maximum content ml	Minimum content ml	Average content ml
1	172	535	525	526.82
2	100	531	529	529

T A B L E I Cont'd

Test No.	Typ. Differ. ml	Variation %
1	2.07	0.39
2	1.96	0.37

The last tests were carried out with pouches or bags 8 having a nominal capacity of 1,000 ml. Results of those tests are set forth in Table II below:

TABLE II.

Number of Pouches Tested	Average content ml	Typical Difference ml	Variation %
200	1036.8	4.78	0.46

The above described tests demonstrate that the variations in pouch content are surprisingly smaller (less than 0.5%) when the apparatus of the invention is used than compared to prior known mechanical devices. Known mechanical devices frequently have variations that reach approximately 10%.

The apparatus of the invention provides a more accurate filling of the pouches, so that the ratio between the internal area of those pouches and the volume of liquid they contain is higher than the corresponding ratio obtained with the known device, for pouches having the same internal area.

The ability to withstand shock of the pouches or bags filled with the apparatus of the invention thus is definitely higher than that of the bags or pouches filled with the known mechanical device.

Claims

1. An apparatus for continuously filling flexible bags or pouches (8) with a perfusion liquid contained in a reservoir (2) that is fed perfusion liquid from a source (3) of such a liquid, that apparatus comprising means to regulate the rate of flow of the perfusion liquid coming out of reservoir (2), as a function of the level of that liquid in that reservoir (2), characterized in that the afore-mentioned regulating means comprise a sensor (15) mounted in the reservoir (2) which sends an electronic signal as a function of the liquid level in reservoir (2), and which is connected to a regulator (16) that continuously regulates the feeding of perfusion liquid to said reservoir as a function of the electronic signal, the sensor (15) and regulator (16) together operating, to maintain the liquid level in reservoir (2) close to a pre-set level.
2. An apparatus according to Claim 1., characterized in that regulator (16) is a regulator with proportional, integral and derivative action, which transforms the signal received from sensor (15) into a signal for governing a member (18) for the feeding of the perfusion liquid to reservoir (2).
3. An apparatus according to Claim 2., characterized in that the above-mentioned member (18) governs a pump (6) for feeding the perfusion liquid to reservoir (2).
4. An apparatus according to Claim 3., characterized in that the above-mentioned member (18) is a device to vary the speed of the pump.
5. An apparatus according to any one of the above claims, characterized in that sensor (15) indicated above is a capacity level sensor.
6. An apparatus according to Claim 1., characterized in that the sensor (15) is connected to a transformer of the signal sent by said sensor (15) into electric current having an intensity ranging between 0 to about 20 milliamperes, which current is sent to regulator (16).
7. An apparatus according to Claims 1 and 3., characterized in that the above-mentioned governing member (18) comprises a converter (19) of the signal coming from regulator (16) into a speed variation of the pump proportional to the rate of flow and to tolerance.
8. An apparatus according to any one of Claims 3 and 4, characterized in that it comprises, downstream from the pump (6) a feeding reservoir (2), and upstream from the latter, a filter (5) designed to hold back the particles contained in the perfusion liquid.
9. An apparatus according to Claims 7 and 8, characterized in that it comprises pressure sensors (2) upstream and downstream from the filter (5), those sensors (20) sending signals to a device (21) that compensates for the loss of charge in the filter (5), said compensating device (21) being mounted upstream from the converter (19) and downstream from the regulator (16).
10. An apparatus according to any one of Claims 3 to 9, characterized in that the pump (6) is a centrifuge

pump.

Revendications

- 5 1. Dispositif pour le remplissage continu de sacs ou poches souples (8) avec un liquide de perfusion contenu dans un réservoir (2) qui est alimenté en liquide de perfusion à partir d'une source (3) d'un tel liquide, ledit dispositif comprenant des moyens de régulation du débit du liquide de perfusion sortant du réservoir (2), en fonction du niveau de ce liquide dans ce réservoir (2), caractérisé en ce que les
10 moyens de régulation précités comprennent un détecteur (15), monté dans le réservoir (2), qui envoie
un signal électronique en fonction du niveau de liquide dans le réservoir (2) et qui est connecté à un
régulateur (16) qui règle continuellement l'amenée de liquide de perfusion audit réservoir en fonction
du signal électronique, le détecteur (15) et le régulateur (16) coopérant pour maintenir le niveau de
liquide dans le réservoir (2) au voisinage d'un niveau prédéterminé.
- 15 2. Dispositif suivant la revendication 1, caractérisé en ce que le régulateur (16) est un régulateur à action proportionnelle, intégrale et dérivée, qui transforme le signal fourni par le détecteur (15) en un signal de pilotage d'un organe (18) d'envoi du liquide de perfusion au réservoir (2).
3. Dispositif suivant la revendication 2, caractérisé en ce que l'organe précité (18) pilote une pompe (6)
20 d'alimentation du réservoir (2) en liquide de perfusion.
4. Dispositif suivant la revendication 3, caractérisé en ce que l'organe précité (18) est un dispositif permettant de faire varier la vitesse de la pompe.
- 25 5. Dispositif suivant l'une quelconque des revendications précédentes, caractérisé en ce que le détecteur précité (15) est un détecteur de niveau capacitif.
6. Dispositif suivant la revendication 1, caractérisé en ce que le détecteur (15) est connecté à un
30 convertisseur du signal fourni par ledit détecteur (15) en un courant électrique ayant une intensité
comprise entre 0 et 20 milliampères environ, ce courant étant envoyé au régulateur (16).
7. Dispositif suivant les revendications 1 et 3, caractérisé en ce que l'élément de pilotage précité (18)
comprend un convertisseur (19) du signal venant du régulateur (16) en une variation de vitesse de la
pompe, proportionnelle au débit et à la tolérance.
- 35 8. Dispositif suivant l'une quelconque des revendications 3 et 4, caractérisé en ce qu'il comprend, en aval de la pompe (6), un réservoir d'alimentation (2) et, en amont de ce dernier, un filtre (5) conçu pour retenir les particules contenues dans le liquide de perfusion.
- 40 9. Dispositif suivant les revendications 7 et 8, caractérisé en ce qu'il comprend des capteurs de pression (2) en amont et en aval du filtre (5), ces capteurs (20) envoyant des signaux à un dispositif (21) qui compense la perte de charge dans le filtre (5), ledit dispositif de compensation (21) étant branché en amont du convertisseur (19) et en aval du régulateur (16).
- 45 10. Dispositif suivant l'une quelconque des revendications 3 à 9, caractérisé en ce que la pompe (6) est une pompe centrifuge.

Patentansprüche

- 50 1. Vorrichtung zum kontinuierlichen Füllen von flexiblen Taschen oder Beuteln (8) mit einer Perfusionsflüssigkeit, die in einem Vorratsbehälter (2) enthalten ist, dem Perfusionsflüssigkeit von einer Quelle (3) für eine solche Flüssigkeit zugeführt wird, wobei die Vorrichtung Einrichtungen aufweist, um die Strömungsgeschwindigkeit der aus dem Vorratsbehälter (2) kommenden Perfusionsflüssigkeit als Funktion des Pegels der Flüssigkeit in dem Vorratsbehälter (2) zu regulieren,
55 dadurch gekennzeichnet,
daß die vorstehend genannten Reguliereinrichtungen einen in dem Vorratsbehälter (2) angebrachten Meßfühler (15) aufweisen, der ein elektronisches Signal als Funktion des Flüssigkeitspegels in dem Vorratsbehälter (2) abgibt und der an einen Regler (16) angeschlossen ist, welcher die Zufuhr von

Perfusionsflüssigkeit zum Vorratsbehälter als Funktion des elektronischen Signals kontinuierlich regelt, wobei der Meßfühler (15) und der Regler (16) so zusammenwirken, daß sie den Flüssigkeitspegel im Vorratsbehälter (2) in der Nähe eines vorher eingestellten Niveaus halten.

- 5 2. Vorrichtung nach Anspruch 1,
dadurch gekennzeichnet,
daß der Regler (16) ein Regler mit proportionaler, integraler und differentiatorischer Wirkung ist und der das vom Meßfühler (15) empfangene Signal in ein Signal zum Regulieren einer Baugruppe (18) für die Zuführung der Perfusionsflüssigkeit zum Vorratsbehälter (2) umwandelt.
- 10 3. Vorrichtung nach Anspruch 2,
dadurch gekennzeichnet,
daß die vorstehend genannte Baugruppe (18) eine Pumpe (6) für die Zuführung der Perfusionsflüssigkeit zum Vorratsbehälter (2) regelt.
- 15 4. Vorrichtung nach Anspruch 3,
dadurch gekennzeichnet,
daß die vorstehend genannte Baugruppe (18) eine Einrichtung zum Ändern der Geschwindigkeit der Pumpe ist.
- 20 5. Vorrichtung nach einem der vorhergehenden Ansprüche,
dadurch gekennzeichnet,
daß der oben angegebene Meßfühler (15) ein kapazitiver Niveausensor ist.
- 25 6. Vorrichtung nach Anspruch 1,
dadurch gekennzeichnet,
daß der Meßfühler (15) mit einem Wandler verbunden ist, der das vom Meßfühler (15) abgegebene Signal in einen elektrischen Strom umsetzt, der eine Stromstärke hat, die zwischen 0 bis etwa 20 Milliampere liegt, und der dem Regler (16) zugeführt wird.
- 30 7. Vorrichtung nach einem der Ansprüche 1 und 3,
dadurch gekennzeichnet,
daß die oben genannte Regulierbaugruppe (18) einen Wandler (19) für das vom Regler (16) kommende Signal aufweist, um es in eine Geschwindigkeitsänderung der Pumpe proportional zur Strömungsgeschwindigkeit und zur Abweichung umzusetzen.
- 35 8. Vorrichtung nach einem der Ansprüche 3 und 4,
dadurch gekennzeichnet,
daß sie stromabwärts von der Pumpe (6) einen Zuführungsvorratsbehälter (2) und stromaufwärts von letzterem einen Filter (5) aufweist, der dazu bestimmt ist, die in der Perfusionsflüssigkeit enthaltenen Partikel zurückzuhalten.
- 40 9. Vorrichtung nach Anspruch 7 und 8,
dadurch gekennzeichnet,
daß sie Druckmeßfühler (20) stromaufwärts und stromabwärts vom Filter (5) aufweist, wobei diese Meßfühler (20) Signale an eine Einrichtung (21) abgeben, die den Ladungsverlust im Filter (5) ausgleicht, wobei diese Ausgleichseinrichtung (21) stromaufwärts vom Wandler (19) und stromabwärts vom Regler (16) angebracht ist.
- 45 10. Vorrichtung nach einem der Ansprüche 3 bis 9,
dadurch gekennzeichnet,
daß die Pumpe (6) eine Zentrifugenpumpe ist.
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